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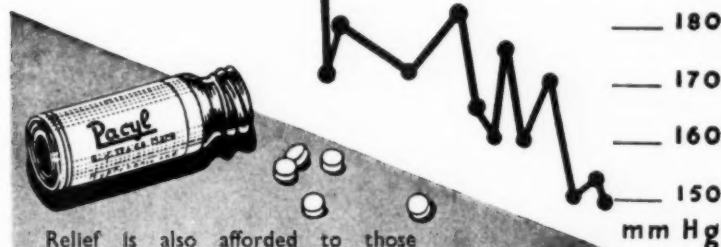
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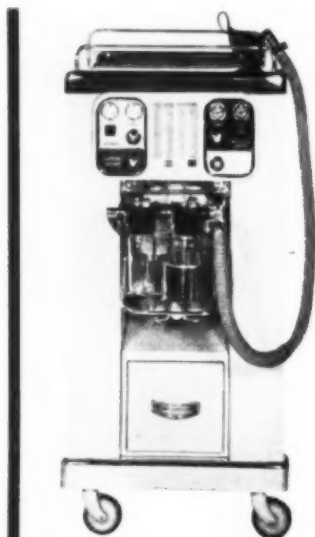
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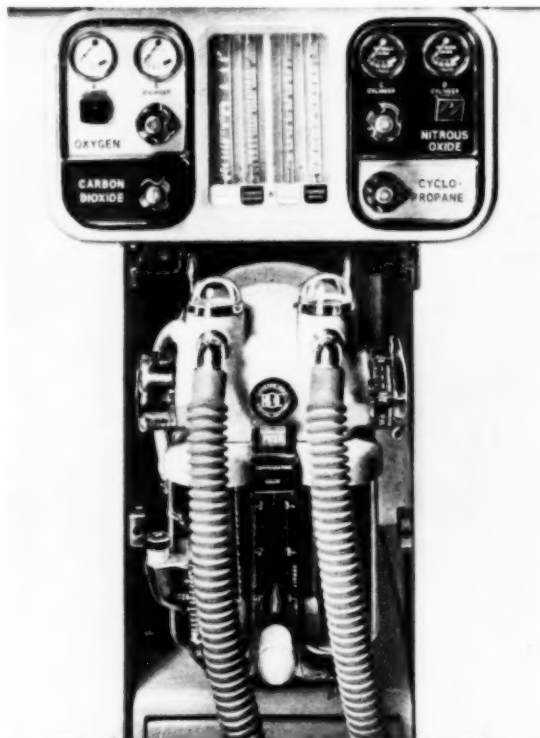
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POLIOMYELITIS IN SOUTH AFRICA

STUDIES IN AN URBAN NATIVE TOWNSHIP DURING A NON-EPIDEMIC YEAR

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During the recent epidemics of poliomyelitis in South Africa, it was noted that relatively more paralytic infections occurred in Europeans than in Bantu. Thus in the 1944-1945 epidemic in the Transvaal, there was an incidence of 40.98 per 100,000 in Europeans, and an incidence of 3.65 per 100,000 in Bantu.¹ In the 1948 epidemic, of the 1925 cases notified, 1,366 were Europeans and 423 were Bantu, giving rates per 100,000 population of 57.57 for the Europeans and 5.40 for the Bantu. It is clear from these figures that poliomyelitis is not uncommon amongst the non-European section of the population of South Africa. It is also clear, however, that the incidence is considerably greater in Europeans. The highest incidence of the disease in the Bantu was in the 0-5 years age group. There were relatively few cases in the older age groups. During the recent epidemic in Johannesburg there were almost as many European cases in the 5-10 age group as in the 0-5 years age group.²

It was suggested that the relatively low incidence of paralytic poliomyelitis in the Bantu and its main incidence on the lowest age group is to some extent, at least, due to an immunity of the older age groups acquired as a result of previous infection.³ As few paralytic cases occur in Bantu infants, it follows that nearly all such infections are silent. It obviously is of considerable importance in the understanding of the epidemiology of poliomyelitis that this hypothesis should be tested.

Two lines of approach present themselves. Firstly, the state of immunity of the different age groups of the different races can be investigated. This can be done by applying the Lansing mouse protection test for the presence of antibodies in the serum of the persons concerned. This test determines immunity to one type of poliomyelitis virus only, but the results will indicate an epidemiological pattern of infection which probably has a wider application.

Secondly, infection with the virus of poliomyelitis may be determined directly by inoculating susceptible monkeys

with a suspension prepared from faeces of the person under observation. If the virus of poliomyelitis is present, the inoculated monkeys will develop characteristic paralysis, and sections of the spinal cord will show typical lesions. Such tests carried out at suitable regular intervals for a long time would detect most infections of poliomyelitis, even though they be silent, in the subjects being studied.

Serological Surveys. The validity of the hypothesis is supported by the results of the serological surveys with the Lansing mouse protection test. These surveys have revealed that in all age groups a greater proportion of Bantu than Europeans have neutralizing antibodies. Indeed, by the time they are six years old, most Bantu children have developed antibodies against the Lansing strain of poliomyelitis virus. These surveys are being continued and expanded and should yield further valuable information. The results will be reported separately.

Isolation of the Virus. An investigation to determine whether this serological immunity is acquired as a result of infection is at present under way in one of the urban Native townships of the Witwatersrand. This paper reports the findings during the first year of observation.

The population of this township is approximately 18,200. There is considerable overcrowding in slum dwellings. Water is supplied by the Rand Water Board and is fully treated and chlorinated at the Board's purification works. There is an open pit system of sewage disposal. Various species of flies are prevalent. In the year ending 30 June 1949, there were 834 births giving a birth rate of 45.8.

The Health Department advises the mothers on infant feeding. Most infants before weaning receive a balanced supplementary diet. However, cases of malignant malnutrition are often seen at the Medical Clinics.

Paralytic cases of poliomyelitis are rare in this location. During the epidemic of 1948 on the Witwatersrand, when over 800 cases were notified in Johannesburg with a

population of approximately 750,000, six cases were notified amongst the 18,200 inhabitants of this location. None has been clinically recognized since October 1948, when this investigation began.

METHOD OF INVESTIGATION

It was arranged to collect specimens of faeces at regular intervals from about 20 infants. The first specimen was collected within a month, usually within 14 days of birth. Subsequent specimens were collected at approximately monthly intervals thereafter. The specimens were transferred from the baby's napkin to a sterile collecting bottle and suspended in 50% glycerin-saline. They were stored for a variable time in a -20°C refrigerator until being prepared for inoculation into the test monkeys.

A 10% suspension of faeces in physiological saline was then prepared and one-fifth volume of pure anaesthetic ether added. The mixture was shaken vigorously and the ether allowed to act for 48 hours. The suspension was then centrifuged in an angle-head centrifuge at 3,000 revolutions per minute for one hour. The fluid of the aqueous phase, now nearly water clear, was withdrawn through the needle into a syringe and about 10 c.c. inoculated intraperitoneally into one monkey of the species *Cercopithecus aethiops pygerythrus* in the case of each specimen. Subsequent specimens from the same baby were inoculated into the same monkey, unless in the meantime it had died of an intercurrent infection or had developed paralytic poliomyelitis. In such cases another monkey was inoculated with the next specimen. Blood was withdrawn from the monkeys by intra-cardiac puncture before each inoculation. The sera separated from these specimens of blood were tested for antibodies against the Lansing strain of poliomyelitis by the mouse protection test.

TABLE I

No.	Initials	Date of Birth	1948				1949										
			Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	April	May	June	July	Aug.	Sept.	Oct.	Nov.	
1	C.N.	13 October 1948	—	—	—	—	—	—	—	—	—	—	BPT				—
2	P.M.	17 October 1948	—	—	Left location	—	—	—	—	—	—	—	—	—	—	—	—
3	E.M.	17 October 1948	—	—	Left location	—	—	—	—	—	—	—	—	—	—	—	—
4	D.T.	3 October 1948	—	—	—	Left location	—	—	—	—	—	—	—	—	—	—	—
5	E.M.	14 October 1948	—	—	Mother refused further specimens				—	—	—	—	—	—	—	—	—
6	B.M.	7 October 1948	—	—	—	—	BPT +	—	—	—	—	—	—	BPT	—	—	—
7	Z.H.	4 October 1948	—	—	—	—	BPT +	—	—	—	—	—	—	BPT	—	VP +	—
8	E.M.	15 October 1948	—	—	—	—	—	—	On holiday	—	—	—	—	BPT	—	VF +	—
9	P.M.	13 October 1948	—	—	—	—	BPT +	—	—	—	—	—	—	—	—	VF	—
10	J.S.	13 October 1948	—	—	Left location	—	—	—	—	—	—	—	—	—	—	—	—
11	G.M.	26 October 1948	—	—	—	—	—	—	—	—	—	—	—	—	—	BPT	—
12	M.M.	29 October 1948	—	—	—	—	—	—	—	—	—	On holiday	—	—	—	BPT	—
13	A.N.	29 October 1948	—	—	—	BPT +	Left location	—	—	—	—	—	—	—	—	—	—
14	M.M.	29 October 1948	—	—	—	—	—	BPT ±	Left location	—	—	—	—	—	—	—	—
15	M.M.	4 November 1948	—	—	—	—	—	—	—	—	Left location	—	—	—	—	—	—
16	D.N.	1 November 1948	—	—	—	—	—	—	—	—	—	On holiday	—	—	—	BPT	—
17	J.M.	4 November 1948	—	—	—	—	Left location	—	—	—	—	—	—	—	—	—	—
18	J.R.	2 November 1948	—	—	—	—	BPT +	—	—	—	Left location	—	—	—	—	—	—
19	J.G.	31 October 1948	—	—	—	—	BPT +	—	—	—	—	—	—	Left location	—	—	—
20	E.V.	21 November 1948	—	—	—	—	BPT +	—	—	—	—	—	—	BPT	—	—	—
21	J.T.	22 November 1948	—	—	—	—	BPT +	—	—	—	—	—	—	BPT	—	Died of intercurrent infection	—
22	B.M.	8 February 1949	—	—	—	—	+ VF	—	—	—	—	—	—	—	—	+ VF	—
23	E.F.	11 February 1949	—	—	—	—	—	Left location	—	—	—	—	—	—	—	BPT	—
24	J.M.	8 February 1949	—	—	—	—	—	—	—	—	—	—	—	—	—	BPT	—
25	B.M.	6 February 1949	—	—	—	—	—	—	—	—	—	—	—	—	—	BPT	—
26	S.M.	2 February 1949	—	—	—	—	—	—	—	—	—	—	—	—	—	BPT	—
27	W.K.	5 February 1949	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
28	M.T.	7 February 1949	—	—	—	—	Left location	—	—	—	—	—	—	—	—	—	—
29	G.M.	6 February 1949	—	—	—	—	—	—	—	—	—	—	—	—	—	BPT	—

VF+ = Virus of poliomyelitis demonstrated in faeces.

BPT - = Lansing mouse protection test on the blood gave a negative result.

BPT + = Lansing mouse protection test on the blood gave a positive result.

Blood samples were also taken from the infants soon after birth, again when they were about six months old and again when they were about one year old. In many instances only one specimen of blood was obtained, due to a natural unwillingness of the parents to allow the infants to have blood withdrawn by venepuncture. This aspect of the investigation remains incomplete, but some results of significance were obtained.

Results of Investigation. The results of the investigation during the first year are summarized in Table I.

COMMENT

It will be noted that of the 21 babies born in October or November only 10 remained in the test for the full year. Most of the others left the location. Only one died during the first year of observation.

The virus of poliomyelitis was demonstrated in the faeces of three of these 10 babies during the year. In one this was demonstrated in the specimen collected in the third month. In the other two the specimen containing the virus was collected during the twelfth month.

Of the eight babies born in February, six remained in the test at the end of November, and the virus of poliomyelitis was demonstrated in the faeces of one of these in the specimen collected during the eighth month. Monthly tests of these babies were continued through to February 1950 to complete the year's observation. No further virus was isolated.

Of the four infants in whose stools the virus of poliomyelitis was detected, the following accounts of their health were obtained from the case records.

J.T., male, was born on 22 November 1948. He was breast fed during the year. In addition he was given supplementary vegetables, cow's milk and maize meal porridge. The virus of poliomyelitis was detected in his stool collected in February, three months after he was born. Up to this time he had had no serious acute illness, but was found to be suffering from congenital syphilis.

He died of enteritis in October 1949. This was the only infant of the 29 under observation, who died during the first year of this investigation.

Z.H., male, was born on 4 October 1949. He was still being breast fed when one year old and was receiving supplementary nutritive, dried milk, maize porridge and vegetables. The specimen of stool collected in October in which the virus of poliomyelitis was detected contained blood and mucus. At the time he was suffering from a condition clinically diagnosed as enteritis. Unfortunately parallel bacteriological investigations were not carried out. It is not possible to say, therefore, whether he had bacterial dysentery at this time. The virus of poliomyelitis was detected in the stool collected in his twelfth month of life.

E.M., female, was born on 15 October 1948. She was still being breast fed when one year old and was receiving supplementary meal, maize porridge and vegetables. She had no serious illness during this time. The virus of poliomyelitis was detected in the specimen of stool in her twelfth month of life.

B.M., female, was born on 8 February 1949. She was still being breast fed at the end of 1949, and was receiving supplementary sour mealie-meal porridge. The virus was detected in the specimen of stool collected when she was eight months old. She had had no illness during this period.

It is apparent from these histories that, if the virus had not been detected by direct tests, infection with the virus of poliomyelitis would never have been suspected. That as many as three of the 16 infants remaining in the test should be infected with the virus of poliomyelitis in the same month indicates clearly that at this time an

epidemic of infection with the virus of poliomyelitis was in progress in the location. Yet careful inquiry by the Medical Officer of Health and his staff failed to find any paralytic cases amongst the several hundred infants in this location. During this year the incidence of poliomyelitis in South Africa was low and no epidemics of poliomyelitis occurred. It is clear from these findings that infection with the virus of poliomyelitis continues to smoulder in such locations even during non-epidemic years.

SEROLOGICAL STUDY

Blood specimens were collected from several infants during the early weeks of their lives. Specimens were collected again when the infants were 6-8 months old, and then again when they were approximately one year old. The sera separated from these specimens of blood were submitted to the Lansing mouse protection test for antibodies against the Lansing strain of poliomyelitis. In these tests to 0.5 c.c. of undiluted serum was added 0.5 c.c. of a 1:10 dilution of suspension of mouse brain infected with the Lansing strain of poliomyelitis virus. The mixtures were thoroughly shaken and then incubated in a water bath at 37° C for two hours. Eight mice were then each inoculated with 0.03 c.c. of the serum-virus mixture intracerebrally.

These mice were observed for three weeks. If five or more survived, the test was considered positive. If two or less survived, the result of the test was negative. If between 2-5 mice survived, the result was deemed to be inconclusive. The results of the Lansing mouse protection tests on the sera separated from these bloods is given in Table II.

TABLE II: PROTECTION TEST RESULTS

No.	Initials	Date of Birth	1	2	3
			1-4 months	6-8 months	12-15 months
1	C.N.	13 October 1948	—	—	—
4	D.T.	3 October 1948	—	—	—
6	B.M.	7 October 1948	—	—	—
7	Z.H.	4 October 1948	—	—	—
8	E.M.	15 October 1948	—	—	—
9	P.M.	13 October 1948	—	—	—
11	G.M.	26 October 1948	—	—	—
12	M.M.	29 October 1948	—	—	—
13	A.N.	29 October 1948	—	—	—
15	M.M.	4 November 1948	—	—	—
16	D.N.	1 November 1948	—	—	—
18	J.R.	2 November 1948	—	—	—
19	J.G.	31 October 1948	—	—	—
20	E.V.	21 November 1948	—	—	—
21	J.T.	22 November 1948	—	—	—
22	B.M.	8 February 1949	—	—	—
24	J.M.	8 February 1949	—	—	—
25	B.M.	6 February 1949	—	—	—
26	S.M.	2 February 1949	—	—	—
27	W.K.	5 February 1949	—	—	—
29	G.M.	6 February 1949	—	—	—

From Table II it is apparent that, for various reasons, this aspect of the investigation could not be carried out completely. However, it does emerge that all sera, except two, collected from infants under four months old gave positive Lansing mouse protection tests. These antibodies

presumably were passively conferred by their mothers, for when some of these infants were again tested at 6-8 months old, they had all lost their protective properties. The two exceptions gave inconclusive results.

The results of the tests on the infants in whom the virus was detected are of special interest. It will be noted that JT, who was infected in his third month of life, when tested for serum antibodies in the same month, was found to give an inconclusive result. When tested again in his ninth month the test gave a negative result. This suggests that his infection was caused by a non-Lansing type of poliomyelitis virus.

Blood from the other three babies, who were found to be infected in October, was collected again in January and February. Two of them now gave positive Lansing protection tests and the other one an inconclusive result. These findings suggest that the virus responsible for the infection at this time was of the Lansing type.

Susceptibility of Rodents to the Virus Strains. To confirm whether these viruses were of the Lansing types, and so pathogenic to rodents, attempts were made to infect rodents. In the first of these, suspensions of the spinal cord removed from the infected monkeys were inoculated into 30-50 mice. These mice were observed for signs of illness and paralysis for a period of six weeks. In the case of the cord of monkey ZH one mouse developed paralysis on the seventh day after inoculation. None of the other mice developed paralysis.

A suspension from the spinal cord of the paralysed mouse was then inoculated intracerebrally into one monkey, which on the twelfth day after inoculation developed severe paralysis. It was killed. Sections of the spinal cord showed the lesions typical of poliomyelitis. At the same time 10 white mice were inoculated, eight of which developed typical paralysis.

An attempt was then made to infect *Mystromys albicaudatus*, one of the common veld rodents of South Africa. Suspensions of the spinal cords from the infected monkeys were prepared as before and then 0.06 c.c. inoculated intracerebrally into 12 laboratory-bred healthy *Mystromys*. In the case of ZH, one of the *Mystromys* so inoculated developed paralysis on the fifteenth day after inoculation. A suspension of the brain and spinal cord from these *Mystromys* was then prepared and inoculated into white mice, one of which developed paralysis resembling that produced by the Lansing virus.

This finding suggests that this common South African rodent may be useful in the study of the virus of poliomyelitis, especially in the differentiation between Lansing and non-Lansing types of virus.

The spinal cord of the paralysed *Mystromys* was then emulsified and inoculated into 12 white mice. One of these became paralysed on the seventh day after inoculation. An emulsion of the brain and spinal cord of this mouse was then inoculated into 18 white mice. Eight of these developed paralysis. These findings are given in tabular form in Table III.

The virus from ZH was then tested by mouse protection tests against sera known to give positive and also against sera known to give negative Lansing mouse protection tests. The results are given in Table IV.

It will be noted that the sera giving protection against

TABLE III: Z. H.

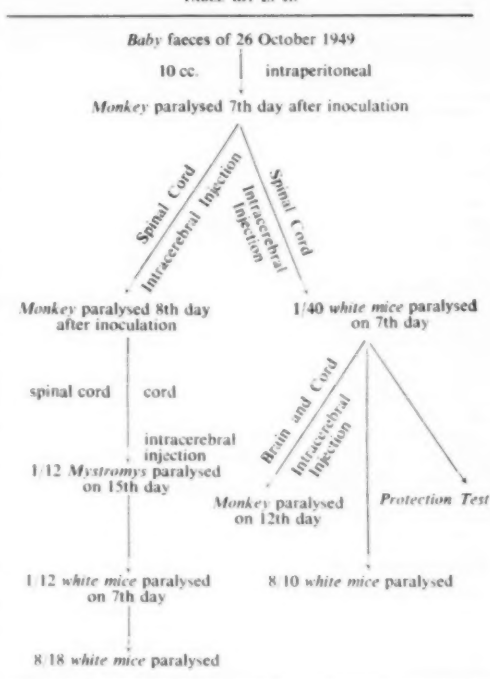


TABLE IV: PROTECTION TEST

Serum No.	Results of Protection		
	Lansing Virus Z.H. Virus		
Lansing positive	1	8/8	8/8
	2	8/8	3/7
	3	7/8	8/8
	4	8/8	7/8
Lansing negative	1	0/8	1/8
	2	0/8	0/8
	3	0/8	1/7
	4	0/8	0/8

the Lansing strain also gave protection against the ZH strain of virus. The sera not giving protection against the Lansing virus also failed to protect against this virus. It has already been noted that the serum from this infant did not protect against the Lansing strain before the infection, while serum collected about three months after infection gave protection. These findings taken together indicate that the virus isolated from ZH was of the Lansing type. Presumably the virus isolated from the other two infants in the same month were also of the Lansing type, although so far this has not been proved

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beyond noting the development in the infants' sera of antibodies against the Lansing strain following infection. On the other hand, the virus isolated from JT in March 1949 was of a non-Lansing type.

COMMENT

This investigation has shown, by direct isolation of the virus, that a considerable proportion of infants may contract an infection with the virus of poliomyelitis during the first year of life. These infections were due in one case to a non-Lansing strain of virus and in three cases to a Lansing type of virus. In the former no antibodies to the Lansing strain subsequently developed in the infant's blood. In two of the latter three cases, the infants developed antibodies against the Lansing strain, whilst in the remaining one an equivocal result was obtained in the mouse protection test. None of the infants infected with the virus had signs or symptoms which could have been recognized as due to the virus of poliomyelitis. Further support is thus given to the hypothesis that the antibodies demonstrable in most older Bantu children have developed in response to a previous, usually silent, infection with a Lansing type of poliomyelitis virus.

It is of considerable interest that four (25%) of 16 infants were proved to be infected with the virus of poliomyelitis during a non-epidemic year, when no cases of clinically recognizable poliomyelitis occurred amongst the 18,200 inhabitants of this Native location.

SUMMARY

It has been noted that Europeans are more liable to paralytic poliomyelitis than the Bantu and that the majority of paralytic cases in the Bantu occur in the 0-5 year age group. It has been suggested that the relatively low incidence of paralytic poliomyelitis in the Bantu and its main incidence on the lowest age group is to some extent due to an immunity of the older age groups acquired as a result of previous infection. This hypothesis is supported by serological surveys which have shown that in all age groups a greater proportion of Bantu than

Europeans have neutralizing antibodies against the Lansing strain of poliomyelitis virus.

To determine whether this serological immunity is developed in response to an infection, a group of Bantu infants born and living in a Native location have been examined for the virus of poliomyelitis at regular monthly intervals. The first test was carried out within two weeks of birth.

Of 29 infants selected 16 have remained under observation for the first full year of this study. Of these 16 infants, four (25%) were proved to be infected with the virus of poliomyelitis during this time. One contracted the infection in the fourth month, one in the eighth month and two in their twelfth month. The virus isolated from the infant in its fourth month proved not to be of the Lansing type. One of the other three was proved to be of the Lansing type. The remaining two were presumably also of the Lansing type.

The infant infected with the non-Lansing virus did not subsequently develop antibodies against the Lansing strain. Two of the infants infected with the Lansing type of virus developed Lansing antibodies following their infection.

It appears, therefore, that the Lansing antibodies demonstrable in the sera of most older Bantu children develop as a result of a previous, usually silent infection with this type of virus. It is significant that four of 16 infants (25%) were proved to be infected with the virus of poliomyelitis during a non-epidemic year, in which no cases of clinically recognizable poliomyelitis occurred amongst the 18,200 inhabitants of this Native location. None of the four infants who were proved to be infected had signs or symptoms suggestive of poliomyelitis at the time of their infection with the virus.

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ABSTRACT

D. S. Ruhe, W. C. Cooper, G. R. Coatney and E. S. Josephson. *Studies in Human Malaria: XV. The Therapeutic Action of Pamaquine (Plasmochin) against St. Elizabeth Strain Vivax Malaria.* Amer. J. Hyg. (1949): 49, pp. 367-373.

The authors wanted to determine whether or not pamaquine was able to cure infections caused by the St. Elizabeth strain of *P. vivax*. White male volunteers were infected by the bites of infected mosquitoes and treated with pamaquine naphthoate during their initial late attacks, i.e. during the first of the wave of late attacks which in this particular strain appears six to 12 months after exposure to infection.

Pamaquine naphthoate was given in tablets of 20 mg., each containing 10 mg. of the base. Quinine sulphate was given in capsules each containing 0.250 gm. of the salt.

Blood smears were examined regularly, until 18 months after exposure.

The following regimens were used: (1) Pamaquine (60 mg. of base per day) for six days, immediately following quinine sulphate, 2 gm. per day, for six days. Four patients received this therapy during the first late relapse; one relapsed again.

(2) Pamaquine (30 mg. of base per day) concurrent with quinine sulphate, 2 gm. per day, for 12 days. None of the six patients relapsed after this treatment of their late primary attack, which followed suppression of early activity by chloroquine.

(3) Pamaquine (60 mg. of base per day) concurrent with quinine sulphate, 2 gm. per day, for 12 days. Seven patients with late primary attacks were treated in this way; none had a relapse.

(4) Pamaquine (90 mg. of base per day) concurrent with quinine sulphate, 2 gm. per day, for 12 days. Six subjects, none of whom relapsed. This group suffered marked cyanosis and abdominal cramps, because the dosage of pamaquine was very high.

No relapse occurred in the 19 patients who received pamaquine and quinine concurrently, but it did occur in one of the four patients who received pamaquine following quinine. This may be contrasted with a 76% relapse rate in alternate case controls and with an overall relapse incidence of 80% in the entire series of initial late attacks given treatment with several other drugs.

South African Medical Journal

Suid-Afrikaanse Tydskrif vir Geneeskunde

VAN DIE REDAKSIE

DIE BESKIKBAARHEID VAN KORTISOON

Dit skyn heeltemal duidelik te wees dat as gevolg van die kritieke internasionale toestand, die uitvoer van Kortisoos uit die Verenigde State uiters streng beperk sal word.

Hierdie hormoon het 'n baie definitiewe inwerking in die geval van veelsoortige patologiese toestande. Daar is taamlik beslis vasgestel dat daar met die gebruik van Kortisoos aangehou moet word in die geval van baie kwale waarop dit op merkwaardige wyse inwerk. In baie gevalle kan die hormoon selfs lewens red en daar kan min twyfel bestaan dat dit vandag as 'n essensiële geneesmiddel beskou moet word.

Aangesien streng uitvoerbeperkings opgelê gaan word, word dit nodig dat die grootste sorg uitgeoefen word by die keur van geskikte gevalle vir behandeling met die geneesmiddel in Suid-Afrika. Alle pogings moet aangewend word om voorrade te bewaar sodat gevalle wat werklik hierdie kragtige vorm van behandeling nodig het, in staat gestel word om die nodige voortsetting van daardie behandeling te geniet.

Die versuim deur geneesheren om so 'n vorm van dissipline en oordeelkundigheid te beoefen kan ongelukkige (en vermybare) tragedies tot gevolg hê; en dit sou hoogs onwenslik wees dat 'n toestand ontwikkel waar die gebruik van Kortisoos deur verordening beperk word tot 'n tabel van spesifiek ingelyste siektes.

Op hierdie stadium is dit belangrik dat navorsings-ondersoeke na die eienskappe van Kortisoos (en trouens ook van ACTH) beperk word tot inrigtings wat toegerus is om hierdie werk te onderneem. Die gebruik van die steroïed-hormoon in private praktyk moet beperk word tot daardie toestande waar die waarde daarvan met 'n mate van sekerheid vasgestel is.

Die hoop bestaan egter dat meer voorrade met verloop van tyd beskikbaar kan word. Alles word in die werk gestel om te verseker dat hierdie land sy volle en redelike kwota ontvang.

VIRUSONTSTEEKING VAN DIE LEWER

'n Onlangse verslag van die kinders-hospitaal van Philadelphia deur dr. Joseph Stokes Jnr. (direkteur van die navorsings-onderneming) maak daarop aanspraak dat minstens twee rasse van die virus wat leverontsteking veroorsaak in baie dele van die wêreld algemeen is.

Die eerste is feitlik uitsluitlik in plasma teenwoordig en dit word deur middel van bloedtransfusies oorgedra. Dit het in die V.S.A. 'n probleem geskep in Bloedbank-programme van die Rooikruis aangesien geen metode gevind is om die aanwezigheid van die siekte in oënskynlik normale persone wat bloed skenk te ontdek nie. Die

EDITORIAL

AVAILABILITY OF CORTISONE

It seems quite clear that as a result of the critical international situation the export of Cortisone from the United States is to be restricted very severely.

This hormone has a most definite action in multifarious pathological states. Its potentialities are by no means known. It is fairly well established, however, that Cortisone must continue to be used in many disorders in which it exerts its remarkable effects. In many instances the hormone may even be life-saving and there can be little doubt that it must be regarded to-day as an essential therapeutic agent.

As stringent export restrictions are being imposed, it becomes necessary for the greatest care to be used in the selection of cases suitable for treatment with this drug in South Africa. Every endeavour should be made to conserve supplies in order to make it possible for the cases which genuinely require this potent form of treatment to be able to have the necessary continuation of that treatment.

The failure of medical practitioners to exercise some such discipline and discrimination may result in unfortunate (and avoidable) tragedies; and it would be most undesirable for a situation to develop in which the use of Cortisone becomes restricted by edict to a catalogue of specifically scheduled diseases.

At this stage it is important that research investigations into the properties of Cortisone (and of ACTH, for that matter) be limited to institutions equipped to undertake this work. The use of this steroid hormone in private practice should be restricted to those conditions in which its value has been established with some certainty.

There is some expectation, however, that increased supplies may become available in due course. Every effort is being made to ensure that this country receives its full and reasonable quota.

VIRAL HEPATITIS

A recent report from the Children's Hospital of Philadelphia by Dr. Joseph Stokes, Jr. (director of the research project) claims that at least two strains of the virus causing hepatitis are prevalent in many parts of the world.

The first one is present almost entirely in plasma and is transmitted through blood transfusions. This has presented a problem in Red Cross Blood Bank programmes in the U.S.A., since no way has been found to detect the disease in seemingly normal persons who donate blood.

Arthritis

and the intestine

Necropsies have shown that there is a greater degree of atrophy of the intestinal mucosa of arthritics as compared with non-arthritics*. This has led to the view that atrophy of the intestinal mucosa could result in deficiencies of vital substances including digestive enzymes. Since the intestine is the site of digestion and absorption, such a condition could lead to an overloading of the blood-stream with undesirable products of incomplete protein digestion.

Based on these observations a method of treatment for rheumatoid arthritis was developed in the preparation Benecol (Benger) which is made from the intestinal mucosa of mammals. Benecol (Benger) is rich in enzymes and standardized on its content of erepsin, a mixture of proteolytic enzymes responsible for the final degradation of protein to amino acids.

It has yet to be proved or disproved that allergy plays an important part in rheumatic conditions, but extensive clinical tests have shown that Benecol (Benger) contains a factor which is successful in the treatment of a high proportion of rheumatic patients.

*Renshaw, A., *Ann. Rheum. Dis.*, 1947, 6. 15.

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tweede ras word deur middel van besmette drinkwater oorgedra. Dié ras is ontwikkel deur middel van kweking in die embrio van die kuiken.

Daar word gehoop dat die gebruik van hierdie medium om die virus te kweek 'n doeltreffende entstof moontlik sal maak as gevolg waarvan persone onvatbaar vir lewerontsteking gemaak kan word. Die voorneme bestaan om die sterkte van die virus te verminder deur opeenvolgende kwekings van die virus oor te ent. Daar is ook werk in verband met 'n huidtoets aan die gang om vas te stel of die persoon waarop dit uitgevoer word vir lewerontsteking vatbaar is en of hy dit al gehad het.

The second strain is communicated through contaminated drinking water. This strain has been developed in chick embryo culture.

It is hoped that the use of this medium for the growth of the virus may make possible the development of an effective vaccine by which persons can be immunized against hepatitis. It is proposed to reduce the strength of the virus through successive cultivations by passage. Work is also proceeding on a skin test to determine whether the subject is susceptible to hepatitis or has had the disease.

THROMBOCYTE COUNTS IN TYPHOID FEVER

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and

R. CASSEL, M.B., B.Ch. (RAND)

Baragwanath Hospital, Johannesburg

According to Drummond (1943) there is a constant and marked fall in the thrombocyte counts in all cases of typhoid fever. He states that this fall occurs early in the disease and often many days before the Widal reaction becomes positive. In his series of 106 cases he found a constant reduction in the platelet count. Figures of 150,000 per c.mm. were not unusual. In six patients the thrombocyte count was between 60,000 and 65,000 per c.mm. In no case in which gastro-intestinal bleeding occurred was the platelet count above 40,000 per c.mm. In two patients with gastro-intestinal haemorrhage, counts of 10,000 and 30,000 per c.mm. respectively, were observed. The bleeding ceased when platelet counts rose above 40,000 per c.mm. No mention is made of the method used in the estimation of the thrombocyte counts.

During a recent outbreak of typhoid fever at Evaton, Transvaal, 40 Bantu patients were admitted to Baragwanath Hospital under our care. An excellent opportunity afforded itself of testing this observation.

Methods. No case has been included which did not conform to one or more of the following criteria:

1. A positive blood or sternal marrow culture.
2. A urine or stool specimen containing typhoid bacilli.
3. A post-mortem examination with findings considered pathognomonic of typhoid infection.
4. A significant or rising agglutinin titre.

Platelets were counted by the direct method using Rees-Ecker diluting fluid. The diluting fluid was drawn in a red cell pipette to the 0.5 mark, and a freely flowing drop of blood from the finger was drawn to the 1.0 mark. The rest of the pipette was then filled to the 101 mark with diluting fluid. After shaking for approximately three minutes a drop was mounted in a standard haemocytometer where the platelets were allowed about 15 minutes to settle and then counted as for a red cell count. The platelets were easily recognized as small dark refractile objects exhibiting Brownian movement. At the

same time blood was withdrawn by venipuncture for estimation of the haemoglobin content using a Klett-Summerson Photo-electric colorimeter.

TABLE I.—PLATELET COUNTS OF EIGHTEEN CASES OF TYPHOID FEVER

Case No.	Platelet Count (1000's per c.mm.)		Haemoglobin (gm. per 100 c.)	Remarks.
	Highest	Lowest		
1	260	200	13.4	Mild case.
2	210	200	12.0	Seriously ill.
3	120	50	8.6	Seriously ill.
4	240	150	14.0	Moderately ill.
5	260	200	14.2	Mild case.
6	430	120	14.2	Moderately ill. Hb. fell to 10.3 gm. when lowest count was obtained.
7	210	200	13.2	Moderately ill.
8	290	170	10.3	Seriously ill. Hb. fell from 11.9 gm. to 9.7 gm. in two weeks.
9	300	140	11.9	Moderately ill.
10	160	130	12.9	Moderately ill.
11	290	90	11.6	Seriously ill. Hb. fell from 13.0 gm. to 11.3 gm. in two weeks.
12	200	180	11.6	Mild case.
13	140	120	12.3	Mild case.
14	250	160	10.6	Moderately ill.
15	320	290	13.0	Died during relapse.
16	—	80*	9.8	Died within four hours of admission. Intestinal haemorrhage. Died on 5th hospital day.
17	90	60	7.3	Died within 36 hours of admission.
18	—	120*	9.6	

* Only one count was done.

Results. Platelet counts were done in 18 cases on alternate days, for a period of 10 to 14 days following admission to hospital. The results are shown in Table 1.

Platelet counts were found to fluctuate widely in individual cases. In only four cases was a significant reduction (below 100,000 per c.mm.) observed. In general, platelet counts followed the haemoglobin content closely. In other words, when an anaemia was present the thrombocytes were also reduced. In six cases the thrombocyte count was less than 150,000 per c.mm. at the time of admission to hospital.

COMMENT

The direct method of counting platelets, as already described, yields counts which are regularly lower than those obtained by some of the indirect methods (Todd and Sandford, 1943). Platelets are difficult to count owing to their property of agglutination and disintegration. Only very great variations in the count have clinical significance.

The results obtained in the present series do not support the contention, postulated by Drummond, that there is an invariable fall in the thrombocyte count in typhoid fever. In only four cases was a significant reduction (below 100,000 per c.mm.) observed. In one case the thrombocyte count was 90,000 per c.mm. shortly before the development of gastro-intestinal bleeding. This patient had also passed blood per rectum on the day before admission.

Platelet counts performed within 24 to 48 hours of admission to hospital exceeded 200,000 per c.mm. in 10 (55.6%) cases. High platelet counts were encountered in moderately ill and in severe cases, while slight reductions were observed in mild cases. The severity of the illness, therefore, appears to bear no direct relationship to the platelet count, except in those cases with profound toxæmia. In these circumstances the bone marrow may be depressed with consequent reduction in leucocytes, erythrocytes and thrombocytes.

SUMMARY AND CONCLUSIONS

We were unable to substantiate the claim that there is a constant fall in the thrombocyte count in typhoid fever. Nor were we able to demonstrate that platelet counts are of value in the early diagnosis of typhoid infections. In only four cases was a significant reduction observed.

We wish to thank Dr. J. Allen, Superintendent of Baragwanath Hospital, for permission to publish this report. We are also indebted to Dr. Margaret Wood for her enthusiastic assistance in the estimation of the thrombocyte counts, and to Dr. J. C. Gilroy and Dr. A. D. Gillanders for their helpful criticism.

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SACCULATED INTERNAL PROLAPSE OF THE VITREOUS

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and

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General Hospital, Johannesburg

Herniation of the vitreous body into the anterior chamber of the eye is known as an internal prolapse. The localized, or sacculated form, following subluxation of the lens, is rare. Sykes and Dodson, who recently described one case, could find no other case reports in the English language and less than 20 cases of this kind reported since Siegfried's description in 1896.

The present writers have recently seen three examples of sacculated internal prolapse of the vitreous. All the patients were the victims of industrial accidents. While Wurdemann, in his 900-page treatise on *Injuries of the Eye*, omits all reference to the condition, the authors feel that this type of lesion must be commoner than the sparse reports would seem to indicate.

CASE REPORTS

1. An adult male was at work when a piece of steel four inches long entered the right orbit, above the eye. Slit-lamp examination revealed a mass of vitreous in the anterior chamber, coming from the nasal side and extending from 1 o'clock to 5 o'clock and nearly to the midline. There was

a clear space between the cornea anteriorly and the vitreous mass. The surface of the vitreous mass was denser than the interior and had the appearance of a membrane. Some brown pigment was scattered on its surface. No displacement of the lens was detected clinically and there was no iridodonesis.

2. An adult male, while at work, ran his left eye against a machine. No abnormality could be detected on naked-eye examination of the anterior segment. With the slit-lamp a vitreous herniation was noted in the anterior chamber, coming from the nasal side of the lens. The prolapse was of an oily, semi-fluid consistency. No condensation of the surface layers was detected. The mass extended from 2 to 5 o'clock and did not reach the midline. The lens did not appear to be displaced and there was no iridodonesis.

3. An adult male alleged that while at work underground he was struck on the left eye by a piece of loose rock. Examination revealed two linear opacities in the anterior substance of the cornea with no evidence of corneal perforation. The iris was tremulous and there was a small posterior dislocation of the lower pole of the lens. At the 4 and 7 o'clock positions at the edge of the pupil were two vitreous prolapses. No condensation of the surface layers was detected. There was some free pigment floating in the anterior chamber. No radio-opaque foreign bodies of the eye could be demonstrated.



CREST

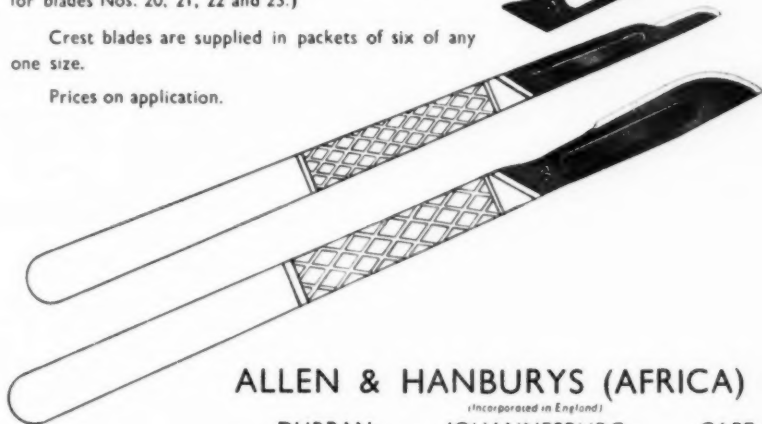
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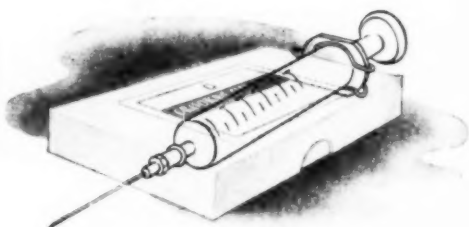
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DISCUSSION

The three cases of vitreous prolapse described were the result of industrial accidents. Severe trauma was the cause of most of the cases described in the literature. A case which seemed to be of spontaneous origin was reported by Hesse. This was in a young boy whose eye was highly myopic and the seat of a retinal detachment.

In two of the cases here described the prolapse was on the nasal side, where the eye is well protected from many forms of direct trauma.

In all the cases it was difficult or impossible to make the diagnosis without examination by the slit-lamp microscope. This makes it possible that the condition is sometimes missed by observers who do not use this instrument.

Internal prolapse of the vitreous may be grouped in three main categories:

1. Following intra-capsular lens extraction.
2. Following dissection of a cataract or after-ataract.
3. After subluxation of the lens.

In the first two cases displacement of the lens could not be detected by the writers. It is probable, however, that a small degree of displacement was present.

The appearance of the prolapse differed in these cases. In the first, a distinct surface membrane was noted. In the second and the third, the vitreous substance was much more fluid in consistency and had no limiting membrane. It is possible that the fluid form of prolapse arises from the primary vitreous in the region of Cloquet's canal.

The mechanism of the production of this type of vitreous prolapse has not been much discussed in the literature. It is evident that the appearance of vitreous in the anterior chamber, in cases of this nature, must be preceded by a solution in the continuity of the zonular ligament. Such a break could theoretically be produced by a force acting either in front of the ligament or behind it. This is illustrated in the two original techniques of intra-capsular extraction described by Smith.

In one of Smith's methods, pressure is applied with a

blunt hook on the cornea, backwards and downwards, as though to insinuate the hook between the edge of the lens and the ciliary body. The ciliary body tends to be pushed down and back and the zonule is torn from its attachment to the lens. Here the operative force comes from the front of the zonule. A rather similar principle is seen in Kirby's technique for producing a subluxation of the lens before intracapsular lens extraction.

In Smith's other technique, pressure is exerted backward on the corneo-scleral margin with a blunt hook placed at 6 o'clock. This produces a forward protrusion of the vitreous at 12 o'clock and causes a tear in the zonule at this site. Harrington believes that in such cases rupture of the zonule is accomplished by the production, by external pressure, of a wedge of vitreous which is made to insert itself between the equator of the lens and the ciliary body. The immediate cause of the tear thus comes from behind.

The writers feel that the mechanics of zonular rupture illustrated in Smith's techniques give a clue to the method in which internal prolapse of the vitreous is produced.

SUMMARY

Three cases of internal saccular prolapse of the vitreous, following on industrial injuries to the eye, are described. Some features of the condition are discussed.

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LABORATORY DIAGNOSIS OF STEROID HORMONE DISEASES*

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Department of Physiology, Medical School, University of Pretoria

With the discovery of adrenocorticotrophic hormone (A.C.T.H.), a protein hormone, and cortisone (Compound E of Kendall—17-hydroxy-11-dehydrocorticosterone), the importance of the endocrines in modern medicine has again been stressed. New vistas have been opened up not only for treatment, but also for the study of the biological mechanisms underlying physiology and disease. Workable and reliable techniques are being standardized for the quantitative evaluation of endocrine states. The chemical structures of the hormones with their metabolites are being studied intensively.

Insulin is a protein hormone as are also the hormones

of the anterior pituitary and of the thyroid gland. The internal secretion of the posterior pituitary is polypeptide in nature, while the hormone of the adrenal medulla may be regarded as a protein derivative. The remaining known hormones, viz. those of the adrenal cortex and the gonads, are steroids and believed to be derived from cholesterol. Cholesterol is widely distributed throughout all living organisms. There is an important biochemical relationship not only between cholesterol and the steroid hormones, but also between other important biological substances such as bile acids, vitamin D, the strophanthus glycosides, digitalis glycosides, the cancer-producing hydrocarbons, and many other substances of biological interest. They are all built about a cyclo-pentano-perhydro-phenanthrene nucleus. The structural relation-

* The References will be published at the end of the concluding part of this paper.

ship between cholesterol and the hormones of the ovaries, testes, adrenal cortex and the bile acids already provides circumstantial evidence that they may be derived from cholesterol; their close relationship with the carcinogens offers the suggestion that they may be converted into these substances during faulty metabolism.

The chief steroid hormones at present of clinical importance are:

The 17-ketosteroids (the C_{19} series of steroid hormones: the total, the ketonic fraction, and the alpha and beta fractions);

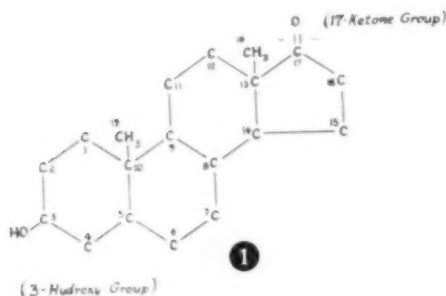
The reducing lipids (the C_{21} series, also called 11-oxysteroids, 11-oxy corticosteroids or 'Cortin', the biological equivalent);

The oestrogens (the total, and the fractions oestradiol, oestrone and oestriol);

Progesterone (with the chief excretion product pregnanediol-3 (α), 20 (α)).

The C_{19} and C_{21} compounds may further be subgrouped in accordance with the number of oxygen atoms inherent in the molecule. In all instances C-11 is either unsubstituted (the 11-desoxy series) or bears a ketonic or alcoholic function (the 11-oxygenated series). Physiologically, this is important, for high gluconeogenic activity (the conversion of protein into sugar), is observed only in the latter group, while marked activity with respect to salt and water metabolism is found only in the desoxy series. Based on the substitution at C-17, the C_{19} compounds fall into a 17-hydroxylated group (e.g. Cortisone) and a group in which the fourth valency bond at C-17 is satisfied with hydrogen (desoxycorticosterone, progesterone, etc.).

The metabolic end-products of some of the adrenal hormones and of the male sex hormones are excreted in the urine as 17-ketosteroids. All androgens are not 17-ketosteroids and all 17-ketosteroids are not androgens; aetiocholan-17-one-3(α)-ol is a 17-ketosteroid but not an androgen, while testosterone has strong androgenic properties, but structurally is not a 17-ketosteroid. The 17-ketosteroids have the following general formula (Fig. 1):



The oxygen atom at C-17 lends itself to the designation of 17-ketosteroid and makes the estimation possible by the Zimmermann procedure in an alkaline metadinitrobenzene solution. A difference in the properties among the 17-ketosteroids is due to the difference in

configuration of the OH-group at C₃; this OH-group may either 'project' above the plane of the paper in one case and below it in the other. These two types of 17-ketosteroids are called 3(β)-OH and 3(α)-OH 17-ketosteroids, formulated respectively by a solid and a dotted valency bond line. The β -OH steroids differ chemically from the α -OH steroids in forming precipitates with the glycoside, digitonin, which are insoluble in 85-90% alcohol. This makes the separation of the two types possible and adds to their diagnostic significance. Normally the β fraction forms from 2% to 10% of the total, but increases to relatively high values in adrenal cortical disease, as with a tumour.

Albright (1947) believes that the 17-ketosteroids are an index of his 'N' (nitrogen) hormone, which is similar to but not identical with testosterone, both in respect of its androgenic and somatotropic properties. His 'S' (sugar) hormone includes compounds such as cortisone, corticosterone, which are responsible for the high gluconeogenesis and diabetes in Cushing's disease (hypophyseal basophilism), the osteoporosis, eosinopenia, lymphocytopenia, muscular weakness, atrophy of the skin, etc., substances which are representative of the 11-oxygenated steroids. A.C.T.H. chiefly stimulates the secretion of 'S' hormones, whereas the luteinizing hormone (L.H.) may be responsible for the production of the 'N' hormones. In the adrenogenital syndrome the 'N' hormones dominate, the children grow much faster than do normal children but, due to early closures of the epiphyses, end up by being normal in height or slightly short. The 'S' and 'N' hormone groups have, therefore, opposite effects; in Addison's disease, a pan-hypo-adrenocorticism, there is a deficiency of both hormones and the skeleton remains virtually unaffected.

Many deviations from the 'N' and 'S' hormone patterns are possible. The salt and water retention hormone (desoxycorticosterone), forms a third and vital group. A case of congenital adrenal hyperplasia (pseudohermaphroditism), has been reported which exhibited increased cortical functions in some respects, but with symptoms of Addison's disease in other respects (Lewis, Klein and Wilkins, 1950).

Physiological activity with respect to carbohydrate metabolism (gluconeogenesis), is dependent upon the presence in the steroid molecule of three functions:

- The α , β -unsaturation in the A-ring; the 3-ketone grouping;
- An alcoholic or ketone oxygen atom substituted in the 11-position;
- The C-20-21 α -ketol side chain (Fig. 2, cortisone).

Reducing power is conferred by (a) and (c) on which depends the determination of the reducing lipids (Heard and Sobel, 1946; Talbot *et al.*, 1945).

Hormonally active corticosteroids may also be assayed biologically (Venning *et al.*, 1946; Eggleston *et al.*, 1946). The estimation is based upon the deposition of glycogen in the liver of adrenalectomized mice and the activity is expressed as the equivalent (in milligrams) of Kendall's compound E (Cortisone) excreted *per diem*—designated as 'E' units. There is a close parallelism between the chemical and biological procedures, although low values, as in Addison's disease or hypopituitarism, are better shown by the biological test (Forbes, Griswold and

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2. As in the case of all new therapies, great care must be exercised in patients suffering from Cardiovascular diseases; patients having less than 85% of normal Liver function; chronic or acute Nephritis; Epilepsy; Diabetes mellitus; Asthma and Pregnancy.
3. "ANTABUS" should not be administered to patients who have been given Paraldehyde as it may be metabolised through an Acetaldehyde stage. Similarly Paraldehyde should not be administered to "ANTABUS"-treated patients.
4. The patients desire to stop treatment should be discouraged until such time as it is confidently felt that social readjustment has been effected. The aid of social workers such as "Alcoholics Anonymous" is, in many cases, of great importance.
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Albright, 1950). The biological test cannot be completely superseded by chemical methods, although cumbersome (Venning, Ripstein and Kazmin, 1949). Many types of excretory products of adrenal cortical origin may retain the power of reduction, but exhibit no biological activity. With increasing age in children the normal adult level is not attained in reducing power as early in life as the output of 'Cortin' (Heard, Sobel and Venning, 1946), facts to be reckoned with in the diagnosis of disease. At the age of seven, when Cortin excretion has already reached adult level, urinary reducing capacity is only 50% of the adult values. In convalescence from injury, the normal biological titre is also attained more rapidly than that of reducing substances.

The rate of excretion of pregnanediol-3(α), 20 α serves as an index of the rate of progesterone formation and metabolism. Progesterone, however, is not the sole metabolic source of pregnanediol, for desoxycorticosterone and other substances can also undergo metabolic transformation into pregnanediol. In cases of adrenal cortical disease the urinary excretion of pregnanediol may be considerably elevated above normal, together with the other steroids. The pregnanediol is excreted as a uronic acid complex, possibly as the sodium salt—sodium pregnanediol-3(α), 20 α glucuronide. This can be weighed as such, but the hydrolysis procedures devised by Astwood and Jones (1941) and modified by Talbot *et al.* (1941), Guterman and Schroeder (1948) and by Somerville, Gough and Marrian (1948) yield better results. It is possible now to follow the excretion during normal menstrual cycles and not only when abnormally high excretions are being encountered.

It is generally believed that α -oestradiol is the chief steroid secreted by the ovary and that it can be metabolized into oestrone, the latter again being converted into oestradiol, and that both can thus be converted into oestriol. The oestrogenic activity of α -oestradiol is about eight to 10 times that of oestrone, and 10 to 15 times that of oestriol when assayed by the vaginal smear method; with chemical (e.g. fluorometric) procedures the values vary somewhat more. The conversion happens chiefly in the liver, which explains the hyperoestrogenism in liver disease, nutritional or otherwise, when this function is disturbed—and the pre-menstrual tension, functional uterine bleeding, cystic mastitis, post-partum subinvolution of the uterus, gynaecomastia and atrophy of the testis, diminished libido and impotence in the male with liver disturbances (Biskind and Biskind, 1942; Biskind, 1946; and others). Such a liver often can still inactivate androgens, and therefore the disturbance in the oestrogen-androgen equilibrium. This explains the therapeutic value of androgens in these cases of functional uterine bleeding, and of the B-vitamins and the lipotropic substances such as methionine and choline (prophylactically or over protracted periods).

It must be remembered that the hormones in the body fluids are mainly water soluble, because they are linked with other chemical groups, such as sulphates or glucuronides. They cannot be extracted directly with organic solvents, such as ether. In the extraction process the first task is, therefore, to break these linkages in order that the hormones may become free and soluble in organic solvents. This can be accomplished by means of

hydrolysis, the urine being boiled with acid. The strength of the acid and time of boiling must be controlled, for heat and acid destroy the free hormones. A detailed discussion of the chemistry of the steroid hormones, together with the procedures recommended for their quantitative estimation, will appear in another paper.

CLINICAL APPLICATION

17-KETOSTEROIDS AND REDUCING LIPIDS

The normal average figures vary according to the procedure used and even in different laboratories for the same procedure, depending upon the completeness of extraction, the extent of destruction and the impurities present. Chromogenic impurities are of secondary importance where a small aliquot is taken for the final estimation, except in special cases. There is serious interference when the quantity of total 17-ketosteroids is low, but then the exact figure is unimportant for most purposes. When the total 17-ketosteroid value is high, differentiation of the excreted steroids into ketonic, non-ketonic and alpha and beta fractions become important; impurities are thus eliminated. Moreover, there is a considerable degree of overlapping of the normal, especially adult values. It is difficult to identify the sex of the donor of a urinary specimen by estimation of urinary 17-ketosteroids alone.

The 17-ketosteroids are excretion products of steroids of which about two-thirds are contributed in the male by the adrenal cortex and one-third by the testis, and possibly the whole by the adrenal cortex in the female. Ovariectomized women show figures within the normal female range as do eunuchs and eunuchoids (about 5 mg. per 24 hours below the normal male average).

The increasing excretion values with increasing age, appear to parallel the curve for the androgens. Both substances present a similar picture in boys and girls with increasing age (Dorfman, 1948). During the first six years of life, extremely low levels of androgenic material are found in the urine. Expressed in terms of equivalents of androsterone and corrected for interfering chromogens (as determined in the purified ketonic fraction), children under six years of age usually excrete less than 1 mg. per 24 hours. The values then rise with a similar rate of increment in boys and girls. This is rather difficult to explain in the presence of the testes in boys. The increase in urinary excretion continues up to about the seventeenth to eighteenth year of life, although figures within the normal adult range may be encountered after the age of 12 years.

In adult women no significant correlation has been reported between the 17-ketosteroid excretion value and the time of the menstrual cycle. The values may range on the average from 8 to 10 mg. or even from 7 to 15 mg. per 24 hours. In pregnancy the values are within the normal range, although higher values (up to 20 mg.) may be obtained in late pregnancy. The climacterium values remain within the normal range, often moderately diminished or moderately increased, indicative of increased functional activity of the adrenal cortex, which may be compensatory.

In adult men the range is from 8 to 20 mg., with an average of 12 to 16 mg. These values remain up to the

age of 50 years and then show a decline as the testes disappear. Older men and women show decreased excretion values.

With such a wide normal range the clinician is safe in regarding as of serious diagnostic significance only figures that tend to shift to twice the normal average or to the zero level. The highest figures are observed in adrenal cortical tumour and the lowest in Simmonds' disease, in which the panhypopituitarism affects both the adrenals and gonads. Values below normal are obligatory in the diagnosis of Addison's disease; fairly low figures are found in advanced cases of Addison's disease in women, but in men under similar conditions the figures are appreciably higher because of the contribution by the testis.

Decreased 17-ketosteroid excretion may be observed in a wide range of debilitating diseases. It may be low in chronic illnesses of all kinds, during the course of acute illnesses, in malnutrition, hypothyroidism, anaemias, anorexia nervosa, malignancy (not involving the endocrine organs); low values are also generally encountered in hepatic disease, diabetes and other conditions without any correlation with the severity of the disease. Lowered metabolism generally accounts for these low values or they may be a reflection of a state of exhaustion (of the adaptation syndrome). Hyperthyroidism also tends to lower the androgen and 17-ketosteroid output in both men and women, probably secondary to non-specific factors such as malnutrition rather than due to a fundamental action of the hormone. It must be remembered that trophic hormones are protein compounds which will suffer when there is a protein lack.

In Cushing's syndrome related to adrenal cortical tumour, the 17-ketosteroid excretion usually (but not always) is increased above the values found for adrenal hyperplasia. This may help to differentiate between the two conditions (Kepler, Sprague, Mason and Power, 1948). High values in the adrenogenital syndrome of 100 mg. or above are likely to be indicative of the presence of a tumour rather than hyperplasia, and are an indication for operative exploration. The estimation of 3 β -hydroxy-17-ketosteroids may be of more help in the diagnosis of adrenal cortical tumour; values of not less than 50% of the total 17-ketosteroids may be a sure sign of this lesion (Callow and Crooke, 1944). Because of the fact that testosterone is not metabolized to dehydroisoandrosterone, the beta 17-ketosteroid, it is believed that the estimation of 3 β -hydroxy-17-ketosteroids may prove to be of value in the differentiation of true interstitial cell tumours of the testis from those conditions which arise from adrenal cortical rests (Prunty, 1950). Chorionepithelioma (and other embryonic tumours) of the testis are associated with normal or decreased 17-ketosteroid values and commonly with high L.H. values.

Precocious puberty resulting from an interstitial cell tumour of the testis may usually be differentiated from that due to an adrenal cortical tumour by the presence of an enlarged testicle. Both will give rise to high 17-ketosteroid values. In precocious puberty due to intracranial tumours (pineal, or in the region of the hypothalamus) the 17-ketosteroid figures usually are normal in the female. It is often accompanied by signs of involvement of the central nervous system (oculomotor

nerve, hearing or spasticity of the limbs). Clinical signs of virilism which may vary from a mild growth of hair on the upper lip to marked hypertrichosis, deepening of the voice and an enlarged clitoris, may be due to an adrenal cortical tumour, pre- or post-pubertal adrenal cortical hyperplasia, a virilizing tumour of the ovary such as an arrhenoblastoma, compensatory adrenal over-activity due to mild ovarian deficiency, or constitutional or racial tendencies. Removal of the tumour is indicated in the first and third conditions and is followed by disappearance of the virilism. Unilateral removal of the adrenal in the other groups will not lead to remission of symptoms. It is therefore important to distinguish between the first and third conditions and the rest, especially if we consider the important function of the adrenal cortex. In arrhenoblastoma of the ovary the 17-ketosteroid values are within or slightly above the normal range. This tumour produces androgenic substances not excreted as 17-ketosteroids. It is, however, possible to palpate the ovarian mass in most advanced cases. Whenever a tumour has been excluded there is no treatment other than depilation or shaving, and operation is not indicated.

In rare instances an adrenal cortical tumour occurring in the male has resulted in gynecomastia, but this can be differentiated from other types, for not only will the oestrogen output be increased, but the 17-ketosteroid output may be very high too. In gynecomastia due to liver disturbances (as in nutritional disease), only the oestrogen (active fractions) output may be raised.

Simmonds' disease is most frequently confused with anorexia nervosa. In the latter condition, however, the 17-ketosteroid as well as the F.S.H. figures never reach the zero levels found in Simmonds' disease, although they are considerably reduced because of malnutrition. Cases of Simmonds' disease without loss of weight may be misdiagnosed as myxoedema. Unfortunately the 17-ketosteroid values can also be low in established cases of hypothyroidism and the 17-ketosteroid estimation is of little assistance in the differential diagnosis. The pigmentation in Addison's disease may help to differentiate this condition from a case of Simmonds' disease. Low 17-ketosteroid values are also obtained in Addison's disease and in the female 17-ketosteroid figures may actually approach zero levels. Tests, as, for example, the elimination of salt from the diet or the ingestion of potassium, are dangerous for they are apt to precipitate a crisis. Other tests in conjunction with the 17-ketosteroids, 11-oxy corticosteroids and blood levels of sodium and potassium such as the ability to produce diuresis and to concentrate chloride and urea (Robinson, Power and Kepler, 1941) may be valuable.

The adrenal cortical function is furthermore tested by its ability to respond to the stimulus of A.C.T.H (Thorn *et al.*, 1948). This would enable us to determine the functional reserve of the organ. Such reserve will be reflected in the increased excretion of 11-oxygenated steroids (reducing lipides), elevated blood sugar levels, increased nitrogen excretion (less constant), consistent increased excretion of uric acid, sustained fall in eosinophil counts, initial decrease in lymphocyte counts (which is not always maintained), extracellular water retention and sodium and chloride retention (especially with prolonged

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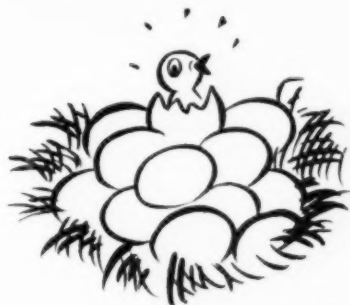
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PETERVITE "B" TABLETS	PETERVITE COMPOUND ELIXIR
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Calc. Pantothenate 2.5 mgm.	Pyridoxine HCl 0.25 mgm.
Pyridoxine HCl 0.25 mgm.	Nicotinamide 5.0 mgm.
Nicotinamide 20.0 mgm.	Liver Extract (concentrate) 15%
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P. 13

Prompt relief . . . prolonged effect

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treatment), and a marked increase in 17-ketosteroid excretion (not likely in the 3 β -hydroxy fraction—Mason *et al.*, 1948). In Addison's disease these changes will vary with the degree of the disease. For a short interval after A.C.T.H. administration (25 mg.) there is little or no change in the creatinine output, in contrast to the sharp rise in the uric acid output, which reaches a maximum four hours after the administration, coincident with the greatest change in the blood count. The uric acid : creatinine ratio (both expressed in mg. per 100 c.c.) is, therefore, used as a means to calculate the adrenal response to different adrenal functional tests.

Thorn and co-workers developed a 4-hour A.C.T.H. test (Forsham, Thorn, Prunty, and Hills, 1948) and a 48-hour test (Thorn and Forsham, 1949), to test adrenal cortical function. The most useful and convenient criteria in the short test are the changes in the eosinophil count and the uric acid excretion. The eosinophil test is independent of kidney changes, but according to Thorn and co-workers it suffers from the disadvantage that certain subjects with allergic eosinophilia may fail to respond, or that occasionally patients may be encountered with eosinopenia due to bone marrow depression. In some cases the uric acid excretion has been found to be less reliable than the eosinophil counts; the uric acid excretion may be approaching its maximum in cases of gout, leukaemia or in decreased renal function; or in some cases of increased adrenal cortical function it may be difficult to increase the excretion thereof. Other factors not yet understood may at times interfere with uric acid responses (Pincus, Hoagland, Freeman and Elmadjian, 1949). It is believed that the excretion of uric acid is dependent upon increased production from broken-down lymphoid tissue, increased uric acid clearance and, under certain conditions, brain cell nucleoprotein may serve as an additional source. In gouty subjects A.C.T.H. is found greatly to increase the clearance of uric acid (Thorn *et al.*, 1949). Increased uric acid excretion, if present, may, however, be regarded as valuable corroborative evidence of adequate adrenal cortical activity.

Patients for the 4-hour tests are not allowed any breakfast, but water is permitted freely, for the ingestion of glucose is known to elicit an adrenal cortical response (increased neutral reducing lipid output, increased uric acid output and lymphocytopenia). With 25 mg. A.C.T.H. a fall of 50% or more in the eosinophil count and an increase of 50% or more in the uric acid : creatinine ratio indicate a good response. In patients with primary Addison's disease these minimum changes are not attained, but in cases of adrenal cortical failure secondary to anterior pituitary deficiency, varying degrees of response may result depending upon the degree of atrophy of the adrenal cortical cells and the severity of their condition.

The 48-hour test allows a longer time for stimulation of the adrenal cortex. Changes in the 17-ketosteroids can also be measured; this will improve the specificity of the test. The patient receives a total dose of 40 mg. of A.C.T.H. per day in doses of 10 mg. at 6-hour intervals, day and night, for two days. An eosinophil count is made before the first dose and four hours after the last one. A 24-hour specimen of urine is collected the day preceding the first injection and a second one during the last 24 hours. A low initial 17-ketosteroid

excretion which fails to rise after A.C.T.H. administration, accompanied by a poor fall in eosinophils (less than 50%), indicates absence of adrenal cortical reserve as is seen in Addison's disease or in hypopituitarism; a low initial 17-ketosteroid excretion which rises after A.C.T.H. administration, with a progressive fall in eosinophils is suggestive of moderate adrenal cortical deficiency due to pituitary failure. Supernormal responses may be obtained in Cushing's disease and acromegaly, depending upon the functional state.

Administration of adrenaline or ephedrine also produces an eosinopenia in the circulating blood, an effect likely to be mediated through the secretion of adrenal cortical 11-oxygenated steroids and dependent upon an intact hypothalamus-hypophysis system (Thorn and Forsham, 1949). Adrenaline is given in a dosage of 0.3 mg. subcutaneously and the eosinophil count done immediately before the test dose and four hours later. Normal subjects respond with a fall of 50% or more in the eosinophil count, whereas neither patients with hypopituitarism nor Addison's disease respond to the test in the normal way. The adrenaline test shows good correlation with the 4-hour A.C.T.H. test and, with the scarcity of A.C.T.H., the adrenaline test may be substituted. The general feeling, however, is that the A.C.T.H. test is to be preferred to the adrenaline test. Unlike A.C.T.H. this dosage of adrenaline does not lead to any marked rise in the urinary 17-ketosteroids or 11-oxycorticosteroids. Pheochromocytoma does not cause an increase in 17-ketosteroid excretion (Koffler *et al.*, 1950.).

The adrenals also respond characteristically to stress (exposure to cold, pursuit-meter operation, post-operative states, burns, etc.) with eosinopenia, lymphocytopenia and steroid changes (Pincus and Hoagland, 1950; Freeman and Elmadjian, 1950). Selye points out that slight increases in steroid hormones may occur in acute illnesses, physical and emotional strain and in post-operative states as a reflection of the participation of the adrenal cortex in the 'alarm reaction'. Shock may be regarded as the initial feature of a severe alarm reaction. The integrity of the hypophysis-adrenal system is essential for the subsequent phase of recovery from shock (counter-shock), which involves increased adrenal cortical function (hyperglycaemia, increased blood chloride, diuresis, increased protein catabolism with a negative N balance and diminished serum potassium and phosphate levels). Adaptation to high temperatures with a high humidity as in the tropics is largely dependent upon the adrenal cortex; among other changes a decrease in the excretion of salt develops.

Psychotic patients, in particular schizophrenics (Worcester Foundation Group), display a striking inability to respond to stress-tests or A.C.T.H. The conclusion was drawn that in every-day life a variety of stresses release in normal persons adrenal cortical hormones that modify a number of metabolic processes, thus reinforcing the body.

The characteristic response of the adrenal cortical cells to stress may prove to be of value in assessing the response of patients to trauma and to operations. With anterior pituitary or adrenal deficiencies (or malnutrition), poor responses can be expected; Thorn and Forsham have

shown that after severe pain, injury and operation there is usually a distinct drop in the eosinophil counts, whereas patients with Addison's disease or hypopituitarism fail to respond. Such tests may prove to be of considerable value to assess the condition of these patients, or the administration of A.C.T.H. in hypopituitarism or in Addison's disease (or the administration of suitable adrenal cortical hormones) before operation, may fortify the patient against risks. The hypophysis-adrenocortical system is an important link in the homeostatic mechanism of the body.

Administration of chorionic gonadotrophin to hypogonadal males may increase the urinary excretion of 17-ketosteroids if the testis is capable of responding; this may be the case in pituitary deficiency. Administration of desoxycorticosterone acetate, in Addison's disease, results in only a very slight increase in urinary 17-ketosteroids. Observations of Polley and Mason (1950) confirmed the view that a 17-hydroxyl group is essential for the metabolic removal of the side chain of pregnane derivatives for the formation of 17-ketosteroids. Increased amounts of 17-ketosteroids were obtained with 11-desoxycortisone (Reichstein's substance S), dihydrocortisone acetate, 17-hydroxyprogesterone, 21-desoxycortisone and with pregnenolone acetate, compounds possessing a 17-hydroxyl group. Exceptions were 17-hydroxycorticosterone and 6-dehydrocortisone acetate. No 17-ketosteroid increases were observed with any of the steroids which do not have a hydroxyl group at carbon 17. Increases in the 11-oxy steroid values were observed when 17-hydroxycorticosterone, 6-dehydrocortisone acetate, 11-desoxycortisone, dihydrocortisone acetate, and 17-hydroxy-11-dehydrocorticosterone (Cortisone or Compound E) were given, steroids with an α -ketol side chain ($\text{CO-CH}_2\text{OH}$).

The identification of reducing lipides (11-oxygenated steroids) may prove to be of value in the differentiation of Cushing's disease (pituitary basophilism) from Cushing's syndrome, which results from primary adrenal cortical over activity. A.C.T.H. chiefly stimulates the production of substances which are excreted as corticosteroids.

By the procedure of Heard, Sobel and Venning (1946), the reducing lipid values for adult males range from 1.1

to 2.1 (average 1.5) mg. per day (calculated as desoxycorticosterone equivalents), and for females from 1.0 to 2.0 (average 1.3) mg. The 11-oxy corticosteroids and 17-ketosteroids were determined in infants from 1 to 11 days of age by Read, Venning and Ripstein (1950). Only small amounts of corticosteroids were found in this age group, showing a definite trend towards higher values with increasing age, but per square metre of body surface the amounts of corticosteroids excreted during the second week of life are of the same order of magnitude as those excreted by normal adults. Relatively large amounts of 17-ketosteroids were found in the first two days of life, followed by a definite downward trend, the values by the ninth day of life being less than one-third of those found originally. Sufficient A.C.T.H. also causes a rise in corticoids, 17-ketosteroids and a fall in blood eosinophils; the responsiveness of the adrenal cortex to A.C.T.H. is found to be increased in the second week of life.

11-oxy steroids as well as 17-ketosteroids show a diurnal rhythm (Pincus, Romanoff and Carlo, 1948, a, b). In the great majority of their subjects they found a minimal excretion of both these types during the sleep period, and a maximal output in the morning, which decreases to less than morning values during the day. The output values were expressed on either a per hour basis, or per gm. of creatinine. Although a similar diurnal pattern of excretion occurs for both types, the changes in excretion (on either a percentage or absolute change basis) of each are not significantly correlated. This indicates that the factors evoking urinary 17-ketosteroid increase (or decrease) are not the same as those evoking neutral reducing lipid change, an implication that the adrenal cortex may secrete 17-ketosteroid precursors independent of neutral reducing lipid precursors. Psychomotor stress in normal men evokes an increased excretion of both 17-ketosteroids and 'Cortin', whereas the administration of glucose an increase in 'Cortin' only. So also in old age neutral reducing lipid values are less affected than the 17-ketosteroids, which indicates that those physiological activities which are influenced by the neutral reducing lipid precursors are constantly maintained in healthy men, whereas the physiological activities influenced by the 17-ketosteroid precursors, diminish in the later decade of life.

(To be concluded)

VERENIGINGSNUUS : ASSOCIATION NEWS

MINUTES OF THE ANNUAL GENERAL MEETING OF THE QUEENSTOWN DIVISION, HELD IN THE FRONTIER HOSPITAL, ON THURSDAY, 25 JANUARY 1951

Present: Drs. Botha, Gardiner, Holmes, Edelstein, Louw, Papilsky, Sapirstein, Schaffer, Schweitzer, Swemmer, Tockar, J. van Schalkwyk, M. van Schalkwyk. *Apology for absence from Dr. Simonsz.*

Dr. Schaffer (Chairman) requested the members to stand in silence for a few minutes in respect and esteem for the late Drs. Rowland and Albertyn. The Chairman welcomed the three new members, Drs. M. van Schalkwyk, Tockar, and Edelstein.

Presidential Address: Dr. Schaffer gave a short review of the meetings and activities of the Queenstown Division during the past year. Eight meetings had been held, mostly clinical. He particularly mentioned the combined meeting and dinner held in April. The President (M.A.S.A.) Dr. Sichel and the Editor of the *Journal* together with members from other Divi-

sions attended. Dr. Waddell gave a most interesting paper at the meeting; and the dinner was a great success. The meeting at the Glen Grey Mission Hospital showed that this Division and the Transkei Branch had common problems—not only matters for ourselves—e.g. tuberculosis of Natives in the Border and Transkei Areas. During the past year the local interns had shown clinical cases very ably and he hoped the present ones would emulate their predecessors.

The Association had had its difficulties during the year; the one with the S.A. Medical Council had been amicably settled.

This year had started with the Cape Hospital Ordinance coming into force. Many matters had to be considered and discussed. The Executive Committee of Federal Council recently met the Liaison Committee (Cape Hospitals) and it was agreed that the honorary staffs of hospitals continue and

be paid an honorarium, the latter to be reviewed from time to time. The Chairman thanked all the members for their loyal support and the Secretary-Treasurer for her services.

Financial Statement: This was perused and passed.
New Members: Dr. Tockar (ordinary member); Drs. M. van Schaikwyk and G. Edelstein (intern members).

Proposed by Dr. J. van Schaikwyk, seconded by Dr. Papilsky.
Election of Officers: President, Dr. R. Schaffer.

At this stage of the meeting the President gave notice of motion: "That a Vice-President be elected and that he automatically becomes President; and that he be designated as President-Elect and Vice-President."

Vice-President: Dr. J. van Schaikwyk.
Honorary Secretary and Treasurer: Dr. D. Holmes.

Executive Committee: Drs. Louw, Swemmer, Papilsky.
Border Branch Representatives: Drs. Louw, J. van Schaikwyk, Gardiner.

General: Dr. Schaffer reported that the Annual General Meeting of the Border Branch will be held in East London on Saturday, 3 February. Dr. Botha questioned the appointment of full-time Housemen in hospitals when it had been agreed that the Honorary Staffs continue as before. He also requested that prior to meetings, a list of the clinical cases to be shown be posted on the notice board at the hospital.

A sincere vote of thanks was passed to the Medical Superintendent and the Matron of the hospital for their hospitality. Tea was served and the meeting terminated at 9.20 p.m.

OFFICIAL ANNOUNCEMENT : AMPTIELIKE AANKONDIGING

FULL-TIME ASSISTANT EDITOR

Applications are invited from bilingual registered medical practitioners for the post of full-time Assistant Editor of the *South African Medical Journal*, on the salary scale of £1,200 x 50—£1,500 per annum, plus cost-of-living allowance at Government rates.

Applicants should state when, if appointed, they would be able to assume duty at the Association's Head Office in Cape Town. The successful applicant will be required to contribute to the Association's Superannuation Fund.

Applications must be lodged with the undersigned (from whom any further information may be obtained) by 12 noon on Saturday, 26 May 1951.

A. H. Tonkin,
Medical Secretary.

Medical House,
P.O. Box 643,
Cape Town,
27 April 1951.

VOLETYDSE ASSISTENT-REDAKTEUR

Aansoeke word gevra van tweetalige geregistreerde geneesherre om die pos van voltydse Assistent-Redakteur vir die *Suid-Afrikaanse Tydskrif vir Geneeskunde*, salaris-skaal van £1,200 x 50—£1,500 per jaar, plus lewenskostoelaag volgens die regeringskaal.

Applikante moet meld wanneer hulle pligte by die Hoofkantoor van die Vereniging in Kaapstad kan aanvaar indien aangestel. Die suksesvolle applikant sal moet bydra tot die Pensioenfonds van die Vereniging.

Aansoeke moet die ondergetekende (van wie verdere inligting verkry kan word) voor 12 middag op Saterdag, 26 Mei 1951 bereik.

A. H. Tonkin,
Mediese Sekretaris.

Mediese Huis,
Posbus 643,
Kaapstad,
27 April 1951.

PASSING EVENTS

We deeply regret to record the death of Dr. A. L. de Jager at the age of 82 years, on 12 April 1951, at Paarl.

The South African National Tuberculosis Association is holding its second Annual Congress on Tuberculosis in Cape Town from 9-11 May 1951.

The conference will be opened by Dr. Karl Bremer, Minister of Health and Social Welfare at 12.15 p.m. on 9 May at the Colosseum Theatre, Cape Town.

Dr. Maxwell Lund, M.B., Ch.B., F.R.C.S. (Ed.) has begun practice as a Specialist Surgeon at 24 Natal Building Society Buildings, Timber Street, Pietermaritzburg. Telephones: Rooms: 5865; Residence: 3498.

The next quarterly meeting of the Christian Medical Fellow-

ship will be held at the Medical School, Mowbray, C.P., on 11 May, at 8 p.m. in the Physiology Lecture Theatre. Prof. Dr. F. Potgieter will speak on: *Does Scripture Refute Evolution?*

HAMILTON-MAYNARD MEMORIAL MEDAL

Mr. Roland A. Krynauw, F.R.C.S., has been awarded the Hamilton-Maynard Memorial Medal for 1950 for his paper entitled *Infantile Hemiplegia Treated by Removal of one Cerebral Hemisphere*. This was published in the *Journal* dated 8 July 1950.

INTERNATIONAL CONGRESS ON ANAESTHESIOLOGY IN PARIS

Any anaesthetist who contemplates attending this Congress is invited to contact the Secretary of the South African Society of Anaesthetists (Dr. Hilda Ginsberg, 155 Highland Road, Kensington, Johannesburg).

IN MEMORIAM

ROBERT BROOM, M.D., F.R.S.

Dr. G. H. Findlay writes: Between 1939 and 1944 I had the privilege of seeing Dr. Broom quite frequently, and I was able to form an impression of the most remarkable scientist I have known. His biography is familiar to many, but what is understood of the man himself?

Perhaps his most striking characteristic was his keenness. His mind seemed to be feeling constantly for a grasp of whatever problem presented itself to him. Dry facts did not exist, because facts were a taunt to his integrative powers. When he devised a theory it was well forged, and one of his delights was always to make it seem less secure than it was. He never seriously claimed that his ideas were right in the paranoid sense, but anybody who differed was challenged to do better if he was able.

Rightness to Dr. Broom was in science what it is in art—that which is aesthetically right. He probably believed that scientific perceptiveness, like artistic awareness, was something that could be taught and acquired up to a point, but beyond this one's feelings were the surest guide. Broom allowed himself scientific licence in a way that enraged and discouraged many individuals. But his influence was never discouraging to those who showed ability, and the names and praises of

his best students from Stellenbosch and his scientific colleagues were ever on his lips.

Just as his thoughts were mobile so was his whole personality. He had known every obstacle and temptation on the ascent to scientific eminence, and he could appreciate in a constructive way just how far along the road a colleague had proceeded. If anyone disliked being 'placed', contact with Broom was not to be recommended. Yet he never despised people who were less able than himself, and I never knew him to be disagreeable towards anybody who might disagree with him. Nevertheless, there were probably people who felt frustrated by his brilliance.

To say of a biologist that he traced out the origin of mammals and the origin of man is practically to say that no greater work could be accomplished. And this was Broom's achievement. It stands on a level comparable with the achievements in physics of men like Clerk Maxwell and Rutherford. To those who knew what mattered in zoology, Broom's work from the 1890's made its mark even then; but in the last few years his researches have received more of the generous and whole-hearted recognition which they deserve. In one sense it is a disgrace that his later honours were so long deferred, but a blessing also that he was alive and active so long as to be able to enjoy them.

BOOK REVIEW

TRIAL OF A SCOTS QUEEN

Trial of Mary Queen of Scots. Edited by A. Francis Stewart. (Pp. 206. With 7 illustrations. Second Edition. 15s.) London: William Hodge and Company, Limited. 1951.

Contents: 1. Prefatory Note. 2. Chronological Table. 3. Introduction. 4. State Trial. 5. Evidence against the Queen of Scots. 6. Justice of Proceedings against Mary. 7. Legality of Proceedings against Mary. 8. Commission for Trying Mary. 9. Examination of Nau and Curie. 10. Documents produced at the Trial of Mary. 11. Intimation of the Impending Trial of the Queen of Scots. 12. Proceedings in Parliament relative to the Sentence on Mary Queen of Scots. 13. Evidence given by Queen Mary's Secretaries. 14. Letter—Sir Francis Walsingham to Sir Edward Stafford. 15. Narration of the Last Days of the Queen of Scots, by Richard Wingfield.

Although there is no specifically medical problem in the *Trial of Mary Queen of Scots*, the reprinting of this remarkable record in the form of a primary source of information will interest the medical practitioner as much as it will interest the layman and the lawyer.

The medical reader, however, will undoubtedly be fascinated by the revelations of the psychological motivation which inspired the deeds and the words of the Queen's accusers.

The proceedings have been reprinted in the form in which they were recorded, thus adding to the value of this historical document, which throws much light on the allegedly female characteristic of Queen Elizabeth's indecisiveness amounting, in this case, almost to duplicity.

CORRESPONDENCE

ACTS PERTAINING TO THE CALLING OF A MEDICAL PRACTITIONER

To the Editor: It is not without interest that I have read the Medico-Legal Section of the *Journal* of 10 February 1951.

Judex has mentioned a number of cases of *Rex versus X.Y.Z.* (people who are held to have performed acts specially pertaining to the calling of a medical practitioner). The selection of these cases, and more so of the judgments, seems rather bewildering to me.

There are, e.g. the two absolutely similar cases of *Rex versus Apter* and *Rex versus Benzie*. The verdict in the first case; *Gultry*; in the latter, *Not Guilty*. It would be of interest to know whether the judgment is based on a law (which law?) or on the judge. Perhaps *Judex* will be good enough to enlighten us on the point.

B. M. Kranz.

Bellevue Street,
Paarl.
11 March 1951.

Judex writes: There is no contradiction between the cases *Rex versus Benzie* (18 E.D.C. 238) and *Rex versus Apter* (1939 N.P.D. 220). The question that arises is always whether the patient paid merely for the medicine or whether he paid also for the diagnosis that preceded the sale. This is essentially a question of evidence. In *Benzie's* case the accused inquired about the symptoms of the child, felt its pulse and looked into its mouth. The Court found that the accused did not charge for doing these acts but merely for the medicine sold. In *Apter's* case a routine was followed. The patients were examined by flashing a torch into their eyes and looking into their eyes and mouths and the accused then advised the patients what medicine to take and sold medicine to them. It should further be mentioned that there were the additional facts that the accused advertised his medicines and that he attended at a given place and at a given time after having advertised in advance that he would be present with medicines to cure or alleviate any ailment. The Court held that the examination, diagnosis and prescription formed a substantial portion of the transaction and were the means employed to induce the last act in the transaction, viz. the actual sale. The examination in *Benzie's* case was an incidental transaction while in *Apter's* case there was systematic diagnosis.—*Editor.*

PLASTIC POCKET NEBULISER

To the Editor: We have received reports that the plastic pocket nebulisers for Antistin-Privine solution or Privine solutions are not working satisfactorily. In the many cases we have investigated, this is due to incorrect handling of the nebuliser itself rather than faulty construction.

After removing the cap the nozzle is inserted into the nostril, the nebuliser being held vertically. It is very essential to apply a sharp, firm pressure by the ball of the thumb in the region of the spot marked on the label to deliver a fine spray of solution. Slow or gentle pressure will not produce a spray.

Distribution of the spray is facilitated by the patient inhaling slightly at the same time. Pressure on the nebuliser should not be released until the nozzle has been withdrawn from the nostril. Under no circumstances should the nebuliser be used horizontally or when tipped downwards, as in these positions a jet of solution is produced.

Ciba Laboratories Limited.

Horsham,
Sussex.

19 March 1951.

SPECIALISTS OR CONSULTANTS?

To the Editor: The letter published on 10 March under the above heading from 'G.P.', who states that he is writing 'as a young general practitioner', makes me smile. It contains—as we used to say in Edinburgh—a lot of 'tripe'. His argument, based on a case which it is alleged was missed by several specialists but proved such a simple one for him to diagnose and heal, seems rather fantastic. But if this story is actually true, then there is no justification whatsoever for any specialist register in South Africa, despite that it contains the names of those whom our highest legislative authority deemed worthy of a higher status either because of special qualifications obtained by examination, or what is even a better qualification: experience in the hard school of medical practice over many years. These qualifications do not appear to be registered against the name of 'young G.P.' even if he believes he can quote the textbooks backwards!

What use would there be for the specialists (who, as 'G.P.' mentions, have all missed such a simple case) to become 'consultants'? Would that improve their practical knowledge by an iota? It would appear that the public does not go to the specialist because the omniscient practitioner of the calibre of 'young G.P.' has given satisfaction. But is it not the right of the patients to choose, even if unwisely, as they so often do, any practitioner, quack or even faith healer? There is no doubt much wrong with our profession in South Africa that even the young G.P. is licensed to tackle anything and everything, while the registered specialist is actually restricted in his work, even if he was formerly a general practitioner of many years' standing enjoying the finest reputation amongst generations. Surely 'young G.P.' will not now castigate his senior colleague who by chance might have been instrumental in his being amongst us, but unable to do the same to him now as then, i.e. slapping him hard on his buttocks, then for not shouting and now because he is shouting.

Medicine cannot and will not be an 'exact' science, but it always was an art, which no young man has had the time to master, whether it is a 'young G.P.' or even a 'specialist'. We are all only human and do make mistakes.

I.R.C.P. & S. (Edin.)

Johannesburg,
29 March 1951.

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TAXOL HAS BOTH THESE ADVANTAGES

Descriptive literature or samples will be sent free of charge to Members of the Medical Profession on application to

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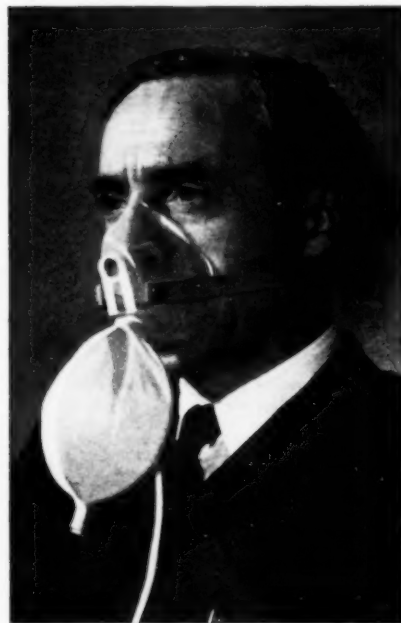
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Dose:—One tablespoonful in water twice or thrice daily.
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The Medical Association of South Africa Die Mediese Vereniging van Suid-Afrika

AGENCY DEPARTMENT : AGENTSAP AFDELING

CAPE TOWN : KAAPSTAD

Medical House, P.O. Box 643, Cape Town. Telephone 2-6177
Mediese Huis, Posbus 643, Kaapstad. Telefoon 2-6177

PRAKTYKE TE KOOP : PRACTICES FOR SALE

(706) Suid-weslike Kaapland naby kus. D.S. aanstelling. Geen opposisie. Premie verlang ongeveer £750. Paaielemente kan gereel word. Huis beskikbaar.

(674) Vennootskapaandeel in Bolandse praktyk. £1,224 gemiddelde netto jaarlikse wins aan aandeel verbonde. Twee aanstellings. Huis te koop, maar is nie 'n voorwaarde vir koop van praktyk nie. Premie verlang £650. Geneesmiddele en sekere spreekkamermeubels ter waarde van £150 word by premie ingesluit. Uitstekende vooruitsigte.

(686) Noord-Kaapland. Medisyne word aangemaak. D.S. aanstelling alleen ongeveer £1,200 p.j. werd. Geen opposisie. Premie verlang £1,500 en dit sluit praktyk, instrumente en meubels in, betaling £750 kontant, balans paaielemente oor een jaar.

(636) Cape Town suburban practice. Non-European. Rental for house £5 p.m. (Quote also 691.)

(511) Vennootskapaandeel in Suidelike Voorstad, Kaapstad. Vennootskapinkomste ongeveer £5,000 per jaar. Twee aanstellings. Afrikaner word verlang. Premie na gelang aandeel wat verkoop word.

PRAKTYKE VERLANG : PRACTICES REQUIRED

(703) Solus or partnership with minimum income of approx. £2,000 p.a., preferably with scope for obstetrics and/or gynaecology, by experienced middle-aged Irish doctor, F.I.C.S. (1946), F.R.C.O.G. (1948).

ASSISTENT, PLAASVERVANGER VERLANG

ASSISTANT, LOCUM REQUIRED

(695) Assistant for approx. 6 months for Natal mixed general practice with D.S. appointment. £90 p.m. if own car provided plus petrol allowance. Lodging provided. Excellent off-duty arrangements.

(559) Locum for Durban practice. From mid May for about 2 weeks. Two and a half guineas p.d. and lodging for locum and his family, plus petrol and oil used by his own car.

JOHANNESBURG

Medical House, 5 Esselen Street. Telephones 44-9134-5
Mediese Huis, Esselenstraat 5. Telefoon 44-9134-5

PRAKTYKE TE KOOP : PRACTICES FOR SALE

(Pr S19) Vrystaat plattelandse praktyk. Totale jaarlikse bruto-ontvangste £2,700. Premie £750.

(Pr S14) Transvaal country practice. Income approx. £1,000 p.a. Transferable appointment held. Premium £500.

(Pr S16) Transvaal hospital town. Income £2,300. No surgery done. Practice is for sale with large house at £5,000.

(Pr S22) Northern Transvaal country practice. D.S. appointment held. Premium £500.

(Pr S23) Progressive practice in S. Rhodesian hospital town. Excellent opportunity for young G.P. Present income £3,000-£4,000 p.a. Premium for goodwill £3,000. Terms accepted. £1,000 for book debts, surgery furniture, drugs, etc. Block of professional rooms and living quarters to rent at £30 p.m.

ASSISTENT VERLANG : ASSISTANT REQUIRED

(A 022) Assistant required for West Rand practice. View to partnership. Applicant must be bilingual gentleman with at least 2 years' experience. Terms during assistantship £2 2s. p.d. plus car allowance and surgery expenses.

ASSISTENTSKAP VERLANG : ASSISTANTSHIP REQUIRED

(A W46) Assistantship with view in English-speaking practice by London-trained doctor, aged 31. Interested in Obstetrics.

(A 024) Doctor required by Insurance Company in South West Africa. Minimum period 6 months. To commence 1 June. Salary £75 per month plus all found, rising to £100 in third month.

Provincial Administration of the Cape of Good Hope

LOVEDALE HOSPITALS: INTERNS

Applications are invited from suitably qualified medical practitioners, European or non-European, for the above-mentioned posts. Duties to commence early in July 1951.

The appointments, which will be for six months on contract in the first instance but may be renewed for a further six months, will be made in terms of, and subject to, the Hospital Board Service Ordinance (No. 19 of 1941) and the regulations framed thereunder.

Salary at the rate of £240 per annum, plus board, quarters and laundry, and cost-of-living allowance at prescribed rates.

These Hospitals, which have a complement of 280 beds for non-European patients, have an establishment of three Senior Medical Officers and five Interns.

The Hospitals are closely associated with Lovedale Missionary Institution, and applicants should be in sympathy with Missionary work.

Applications should be addressed as soon as possible to:—

The Medical Superintendent
Lovedale Hospitals
P.O. Lovedale, C.P.

City of Kimberley

LOCATIONS MEDICAL OFFICER

Applications are hereby invited from qualified registered medical practitioners for the post of Medical Officer (Clinical) in the Council's Native Locations on the grade £600—£800 per annum plus temporary cost-of-living allowance. Transport will be provided by the City Council.

The successful applicant will be in charge of the Locations Medical and Nursing Service, under the jurisdiction of the Medical Officer of Health and will carry out such duties as the Medical Officer of Health may determine.

Applications, stating age, qualifications, experience and the earliest date duty can be assumed and accompanied by copies of not more than three recent testimonials, must reach the undersigned not later than Monday, 14 May 1951.

R. Hartley Marriott
Town Clerk
(65/1951)

Town Office, Kimberley
16 April 1951

Hairdressing Trade Sick Benefit Fund

Applications are invited for the following part-time post: Medical officer for the Brakpan Area.

Applications must reach the undersigned not later than 19 May 1951.

Further details can be obtained from the Secretary, P.O. Box 1201, Johannesburg.

Wanted

Energetic and experienced general practitioner capable of doing general surgery in partnership practice in large country hospital town with all facilities. One partner proceeding overseas for further study. Either long-term locum, or purchase of share of practice to be arranged. Good opportunity for Jewish doctor. Write stating particulars of experience, marital status, and when able to commence to 'A. G. C.', P.O. Box 643, Cape Town.

Medical Officer

Applications are invited for a part-time medical officer for a Benefit Society, area Wynberg tram terminus to Lakeside including Southfield and adjoining areas.

Applications for information and appointment should be addressed to the Secretary, P.O. Box 2614, Cape Town by 15 May 1951.

Required

Industrial concern requires a part-time medical officer to attend to their staff. Apply to 'A. G. H.', P.O. Box 643, Cape Town.

Siekelonds van die Suid-Afrikaanse Spoorweë en Hawens

AANSTELLING VAN SPOORWEGDOKTER: FICKSBURG

Applikasies word van geregistreerde mediese praktisyns ingewag vir die betrekking van Spoorwegdokter, Ficksburg en vir die spoorweglyntrajek tot by Fournesburg (uitsluitend) teen 'n salaris van £202 per jaar, plus die geide en toelaes wat in die regulasies van die Siekelonds voorgeskryf word, en met die reg om privaat te praktiseer.

Die salaris is onderhewig aan wysiging in ooreenstemming met die sensus van lede wat op 1 April van elke jaar afgeneem moet word.

Die aanstelling geskied kragtens die regulasies van die Siekelonds en opsegging van diensie is onderworpe aan vier maande kennisgewing deur een van beide partye.

Die suksesvolle applikant moet in Ficksburg woon, diens aanvaar op 'n datum wat gereel sal word, en sy pligte ooreenkomstig die regulasies van die Siekelonds uitvoer.

Aansoeke moet die Distriksekretaris, Distriksiekelondsraad, Charlesstraat 2, Bloemfontein, nie later as 26 Mei 1951, bereik en die applikante moet die volgende vermeld:

1. Volle naam.
2. Kwalifikasies (waar en wanneer verkry en opgedoen).
3. Ondervinding (waar en wanneer verkry en opgedoen).
4. Datum van geboorte.
5. Land van geboorte.
6. Getroud of ongetroud.
7. Of ten volle tweetalig.
8. Of Suid-Afrikaanse burger is.
9. Watter staatsbetrekking, indien enige, beklee word.
10. Wering deur en ten behoeve van enige applikant stel so 'n applikant bloot aan diskaualifikasie.

Enige verdere besonderhede wat verlang word, kan op aanvraag van die Distriksekretaris by bovermelde adres verkry word.

P. J. Klem

Johannesburg
5 Mei 1951

Hoofsekretaris
(87)

Public Service Commission

VACANCIES IN THE PUBLIC SERVICE

1. The attention of medical practitioners, registered with the South African Medical and Dental Council, is drawn to an advertisement appearing in the *Government and Provincial Gazette* of this week, inviting applications for posts of Medical Officer (salary scale £960-£40—£1,120) in the Department of Health.

2. In addition to salary a cost-of-living allowance of £256 for married officers and £80 for unmarried persons is payable for the present.

3. It is emphasized that full and detailed particulars of qualifications and previous experience (including military service) must be furnished but original certificates and testimonials should not be submitted. Application forms (Z. 83 and P.S.C. 8 (a)) are obtainable from the Secretary, Public Service Commission, Pretoria, to whom filled-in forms must be addressed.

4. The closing date for the receipt of applications is 26 May 1951.

(28565)

Assistantship Required

A well-experienced, English-speaking general practitioner; married; T.T.; qualified Edinburgh 1941; bilingual; studied F.R.C.S. unsuccessfully. Practical surgery for the last 3 years. Has held a registrar's post, general, gynaecological and orthopaedic surgery. Excellent testimonials. Returning to South Africa on 31 May 1951. Desires assistantship general practice with a view to partnership, preferably at or near the coast. Capital available. Reply to 'A. F. R.', P.O. Box 643, Cape Town.

Natal Provincial Administration

VACANCIES FOR SENIOR MEDICAL OFFICERS

Applications are invited from registered medical practitioners for appointment to a vacant post of Senior Medical Officer in the Natal Provincial Administration as under:—

1. Addington Hospital, Durban: Department of Ophthalmology.
2. Addington Hospital, Durban: Department of Gynaecology and Obstetrics.
3. Grey's Hospital, Pietermaritzburg: General Duties.
4. Wentworth and King Edward VIII Hospitals, Durban: Department of Venereal Diseases.
5. King Edward VIII Hospital, Durban: Department of Medicine (2 vacant posts).
6. King Edward VIII Hospital, Durban: Department of Surgery.
7. King Edward VIII Hospital, Durban: Department of Orthopaedics.

The appointment is on 12 months' contract and the salary is as follows:—

- A. Two years' service after qualification—£400 per annum all found.
- B. Three years' service after qualification—£600 per annum plus free quarters or an allowance in lieu thereof.
- C. Four years' service after qualification—£700 per annum plus free quarters or an allowance in lieu thereof.
- D. Five years' service after qualification—£800 per annum plus free quarters or an allowance in lieu thereof.

Applications should be addressed to the Director of Provincial Medical and Health Services, P.O. Box 20, Pietermaritzburg, to reach him before 16 May 1951.

(AD 6234)

Motor Industry Sick Benefit Fund

(TRANSVAAL AND ORANGE FREE STATE)

(PART-TIME MEDICAL OFFICER FOR BARBERTON)

Applications are invited from fully qualified registered general practitioners in respect of the abovementioned appointment.

The Fund operates on the closed panel system and the successful candidate will be required to provide consulting room, domiciliary and hospital service (when necessary) for members and their dependants. Further details will be furnished on request.

Applications must reach the Secretary of the Fund, P.O. Box 8477, Johannesburg, by Wednesday, 23 May 1951.

(17 April 1951)

Vanderbijl Park Estate Company

VACANCIES: SPECIALIST-PHYSICIAN AND SPECIALIST-SURGEON

Applications are invited from registered physician-specialists and specialist-surgeons for the above positions.

The successful applicants will be required to obtain a satisfactory Certificate of Health from the Company's Medical Officer and the appointment will be subject to the Company's Conditions of Service.

Applications should be addressed to the undersigned, P.O. Box 1, Vanderbijl Park, not later than 19 May 1951, and the successful applicants will be required to assume duty on or before 5 July 1951.

Application forms together with full particulars regarding the positions will be addressed to *bona fide* applicants on written application to the undersigned.

Colin L. Harris

16 April 1951

Secretary

For Sale

Native Clinic in Northern Natal. For particulars apply to H. C. Briscoe, Mount Prospect, Natal.

**Decongestion-
Bacteriostasis
in Nasal and Sinus
Infections**

*** NEO-SYNEPHRINE**
Sulfathiazolate, 0.6%

Presents

2 *outstanding agents
of established value in
topical intranasal
therapy.*

BACTERIOSTAT + VASOCONSTRICTOR

Rapid decongestion with undiminished effectiveness is combined with proven bacteriostasis in Neo-Synephrine Sulfathiazolate, 0.6%. Two or three drops in each nostril every three or four hours will provide relief in nasal and sinus infections. On prescription, in 1-oz. bottle, with dropper, and also 16-oz. bottles.

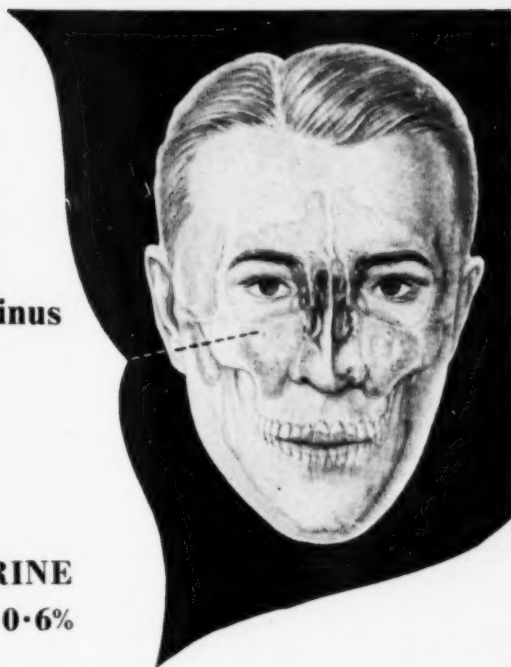
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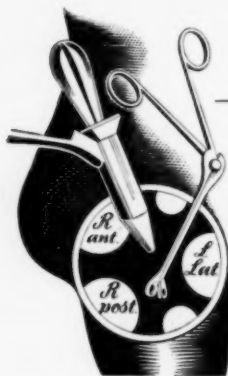
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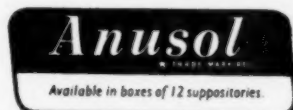


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Anusol is also available in Ointment form



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STIGMINENE BROMIDE 'Warner' is indicated in the prevention and treatment of post-operative abdominal distention and urinary retention. It may be used for all degrees of intestinal and urinary bladder atony: ranging from gastro-intestinal atony developing in chronic illness, certain acute infections or toxæmias, following anaesthesia; through meteorism complicating pneumonia, to as severe an involvement as paralytic ileus.

STIGMINENE BROMIDE 'Warner' is supplied in 1-cc ampoules of a 1:2000 solution, 0.5 mg. each; cartons of 6 and 50 ampoules.

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